

February 13, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16146-review.doc).

**Title:** Effect of endogenous CCK on the course of acute pancreatitis in rats

**Author:** Dongmei Jia, Mitsuyoshi Yamamoto, Makoto Otsuki

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 16146

I appreciate all the constructive comments of the reviewers and the opportunity to submit a revised version of my manuscript entitled, “**Effect of endogenous CCK on the course of acute pancreatitis in rats**”.

I carefully revised my manuscript in accordance with all the comments raised. My point-by-point responses to the reviewers’ comments are shown below. The corresponding changes in the revised paper are underlined.

The revised manuscript was also thoroughly checked and edited by a native English-speaking medical editor to meet the language standards required by leading English language publications.

I hope that the revisions made have satisfactorily answered all the comments raised and that our paper is now suitable for publication in the *World Journal of Gastroenterology*.

Thank you in advance for considering our revised paper for publication.

I look forward to hearing from you at your earliest convenience.

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) **Reviewed by 00070291 :**

1. Acute pancreatitis was induced by infusing 40μl/100 g body weight of 3% sodium taurocholate sodium salt. Thank you for your suggestion.
2. We revised the running tittle. The new title is “strategy for acute pancreatitis recovery”.

(2) **Reviewed by 02841861**

1. We revised the running tittle. The new title is “strategy for acute pancreatitis recovery”
2. We revised English language and style according to your suggested remarks in the manuscript.
3. My colleague at the Washington University in St. Louis School of Medicine had proof read the manuscript and she agreed to give her name (Lauren Schellhardt) and e-mail address ([schellhardtl@wudosis.wustl.edu](mailto:schellhardtl@wudosis.wustl.edu)) in case you and editorial office need to contact with her.

(3) **Reviewed by 02439200**

1. The reviewer’s question is very important. We are very sorry but we did not perform the

experiment with the pancreatic rest for the first 5 days followed by standard rat diet. We assumed that the proposed treatment is better than feeding ad libitum without any treatment or pancreatic rest for 10 days, but might be worse than the treatment with 5 day rest followed by stimulation. Pancreatic stimulation is important for the regeneration of the damaged pancreas.

**(4) Reviewed by 00069230.....**

1- Endogenous CCK at different time points must be measured in all the groups and results should be included.

I really agree with the reviewer's comments. We determined plasma CCK levels at several time points as a preliminary study in only limited number of rats. We will try to increase the number of experiments so as to be able to perform statistical analysis in our next study. Thank you for your suggestion.

2- Measurement of severity parameters in serum and pancreatic tissue should be included for the same time points mentioned in point 1. These parameters comprise myeloperoxidase (MPO), TNF- $\alpha$ , IL-6, lactic dehydrogenase (LDH), and C-reactive protein (CRP).

I agree with reviewer's comment. It is ideal to determine all of these parameters in serum and pancreatic tissue at different time points. However, we could not do them. We assumed that the absence of infiltration of inflammatory cells, and expression of TNF- $\alpha$  and IL-1 $\beta$  in the pancreas at final stage (at the end of our study) is good enough for our conclusion. We think about your comments for our next study. Thank you for your suggestion.

3- For a difference amongst treatments to enable extrapolation of such a conclusion, this difference must qualify as a significant difference.

I agree with the reviewer's comment. Unfortunately, we could not get statistically significant difference between AP-R/S and AP-S. Since, however, there was a trend that bombesin-stimulated pancreatic exocrine response in AP-R/S rats is higher than in AP-S rats, we would like to say that pancreatic rest followed by stimulation is "favorable strategy" for the treatment of acute pancreatitis.

4- It would be relevant to include in the Discussion section, the results obtained by Song W et al (Song W, Yamaguchi H, Nakano I, Kimura T, Nawata H. Role of endogenous cholecystokinin in the regeneration of pancreatic tissue after acute hemorrhagic pancreatitis in rats. *Fukuoka Igaku Zasshi*. 1996; 87(1): 14-22), which also study the effects of camostat and a CCK-receptor antagonist on pancreatic regeneration after acute hemorrhagic pancreatitis.

Thank you for suggesting a good study by Song et al. I included their results in our discussion (page 17, lines 5-9) and cited the manuscript as Reference 50.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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